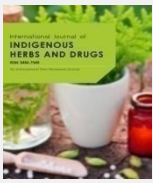
Review Article

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PHYTOSOMES: BRIDGING HERBAL MEDICINE AND MODERN DRUG DELIVERY TECHNOLOGY

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ABSTRACT

Phytosomes are novel phospholipid drug delivery mechanisms that enhance absorption, bioavailability and therapeutic efficacy of plant-derived bioactive constituents. Herbal medications include multiple pharmacologically active phytoconstituents but their clinical efficacy may be hindered by their low water solubility, limited intestinal permeability, chemical instability and substantial first-pass metabolism. Phytosome technology overcomes these problems via the formation of molecular complexes of phospholipids, especially phosphatidylcholine and standardized plant extracts or separated phytoconstituents. Such complexes may improve the interactions with biological membranes and the transport of certain phytochemicals. Phytosomes are gaining significant attention of the researchers for their possible role in the treatment of inflammatory illnesses, liver disorders, cardiovascular diseases, metabolic disorders, skin diseases and cancer. They are also being studied for use in nutraceuticals, cosmetics, and topical formulations. This review speaks about the basic concepts, formulation strategies, latest research, benefits, drawbacks, limits and therapeutic uses of phytosomes. Formulation characterisation, stability, manufacturing problems, safety and clinical translation are all discussed in detail. Despite encouraging experimental and some clinical data, the advantages of phytosomes rely on the phytoconstituent, composition of the formulation and the mode of administration. More standardized research, large-scale manufacturing studies, and well-designed clinical trials are needed to determine their long-term safety, effectiveness, and commercial viability. Phytosomes provide a viable approach to combine traditional herbal treatment and current pharmaceutical technologies.

Keywords: *Phytosomes, herbal medicine, phospholipid complexes, novel drug delivery systems, phytoconstituents, bioavailability, phosphatidylcholine, nanomedicine, therapeutic applications.*

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INTRODUCTION

Medicinal plants have been employed for ages in traditional healthcare systems and are valuable sources of biologically active chemicals [1]. Phytoconstituents including flavonoids, polyphenols, terpenoids, glycosides and other plant-based compounds have shown antioxidant, anti-inflammatory, antibacterial, hepatoprotective and other pharmacological properties [2]. However, the physicochemical and pharmacokinetic characteristics of herbal substances sometimes limit their development into successful pharmaceutical medicines [3]. Poor water solubility, poor membrane permeability, degradation in the gastrointestinal tract and quick metabolism can decrease the quantity of active chemical reaching the systemic circulation [4]. Traditional herbal products such as powder, extracts, pills and capsules may not always give the best absorption of their active ingredients [5]. Thus, the contemporary pharmaceutical research has been concentrated on the development of innovative drug delivery mechanisms that can increase the stability, absorption and therapeutic effectiveness of phytochemicals [6]. One such method is the use of phytosomes [7]. These are generated by complexation of plant derived active chemicals or standardized extracts

with phospholipids, mainly phosphatidylcholine [8]. Phytosome technique is different from typical formulations in which a plant extract is simply mixed with a lipid carrier [7, 9], since it entails specialized molecular interactions between appropriate phytoconstituents and the polar head of the phospholipid. These interactions are able to change the physicochemical properties of the active substances and increase their compatibility with biological membranes [10-11].

Matias et al. examined phytosomes as biocompatible carriers for natural medicines. Their review included interactions between natural chemicals and phospholipids, manufacturing techniques and oral and topical treatments. They emphasized the potential of phytosomes to solve the solubility and stability problems of natural chemicals [12]. Lu et al. in the study of phyto-phospholipid complexes, with attention on the selection of active ingredients, phospholipids, solvents and molar ratios. They reviewed molecular interactions, structural verification, production methodologies and evidence of enhanced bioavailability for several chosen compounds [13]. Barani et al. published a review on the application of phytosomes as delivery methods for phytochemicals. In their review they discussed formulation principles and experimental and clinical data in a number of therapeutic domains with special emphasis on curcumin and silymarin formulations [7].

Studies on phytosomes for topical administration have studied their capacity to enhance the interaction of phytochemicals with skin barrier [9]. Such technologies are being researched in dermatological formulations, administration of antioxidants and in local anti-inflammatory applications. The results rely on the active substance, the skin model and the properties of the formulation [14].

The present review emphasizes phytosomes as a novel platform for phytopharmaceuticals. It discussed therapeutic and clinical uses and highlighted stability, large scale manufacture, regulatory constraints and limited clinical translation as major obstacles [15, 16]. Overall, the research suggests that phytosomes are a promising formulation method. But much of the information comes from laboratory research, animal studies and narrative reviews [7]. The level of the clinical evidence varies greatly between particular formulations and indications. The phytosome method has been investigated for silybin from milk thistle, curcuminoids from turmeric, green tea polyphenols and other plant-derived bioactives [17, 18]. It has been demonstrated that suitably designed phospholipid complexes may increase the bioavailability of some phytoconstituents relative to their non-complexed counterparts [13, 19]. The increased interest in phytosomes shows the necessity to integrate traditional herbal treatment with modern pharmaceutical development [20]. However, better absorption does not necessarily translate into better clinical result. Specific information on formulation, consistent production, safety evaluation and controlled clinical investigations are still needed to translate laboratory discoveries into reliable medicinal medicines. This study looked at the definition, structure and composition, mechanism of action, benefits, drawbacks, limits, challenges,preparation methods, applications, and future prospects of phytosome technology as a new method to herbal medication administration.

Definition

Phytosomes are phospholipids and bioactive compounds from plants, produced by the interaction of appropriate bioactive chemicals of plant origin with phospholipids [21]. Phosphatidylcholine is frequently employed because to the presence of its hydrophilic and lipophilic domains, allowing interaction with phytoconstituents and lipid-rich cellular membranes [22]. The word phytosome is used commonly to refer to phospholipid-based herbal delivery solutions. The method is founded on molecular complexation rather than simple entrapment of an extract within a typical lipid vesicle [19, 23].

Structure and Composition

A typical phytosome formulation includes the following components: (a) a phytoconstituent or standardized extract, such as silybin, curcumin, or flavonoids; (b) a phospholipid, typically phosphatidylcholine; (c) a suitable solvent that is used during the preparation process and is subsequently removed or controlled; and (d) optional excipients, which may include stabilizers, antioxidants, or surfactants, depending on the dosage form [24].

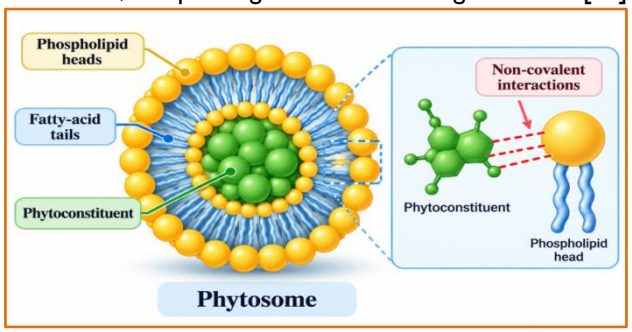


Figure 01:Structure and composition of phytosome

Hydrogen bonding and other non-covalent interactions occur between appropriate phytoconstituents and phospholipids' polar head regions. Lipid chains help the complex interact with lipid surroundings [25].

MECHANISM OF ACTION

Complex formation: Interactions between the phytoconstituent and phospholipid produce a complex with altered physicochemical properties [26].

Improved membrane interaction: The lipid component can enhance compatibility with biological membranes and facilitate absorption of selected compounds [27].

Potential protection from degradation: Complexation may reduce exposure of susceptible phytochemicals to environmental or gastrointestinal degradation [28].

Improved pharmacokinetic performance: Depending on the compound, formulation, and route, phytosomes may increase systemic exposure or prolong the presence of active constituents in the body [29].

Potential improvement in local delivery: Topical phytosomes may increase interaction with skin lipids and support delivery into skin layers [28]. These mechanisms are formulation-dependent. Phytosomes do not invariably improve aqueous solubility, protect every active compound, or produce targeted delivery to a particular organ [30].

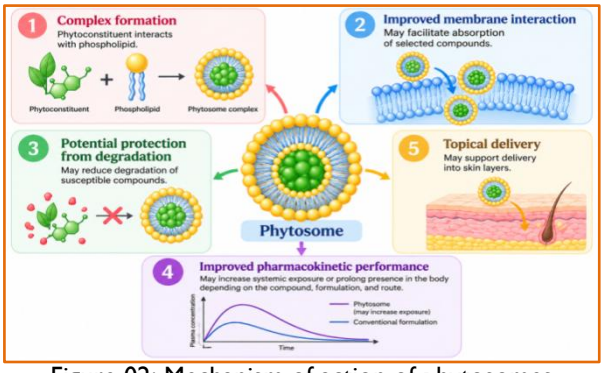


Figure 02: Mechanism of action of phytosomes

Advantages

Improved Bioavailability: Improve the absorption of selected phytoconstituents by modifying their interaction with biological membranes. This is especially relevant for compounds with limited oral absorption [31, 32].

Enhanced Membrane Permeability: The phospholipid component can improve compatibility with lipid-rich biological barriers, potentially facilitating absorption of phytochemicals that otherwise exhibit limited permeability [33].

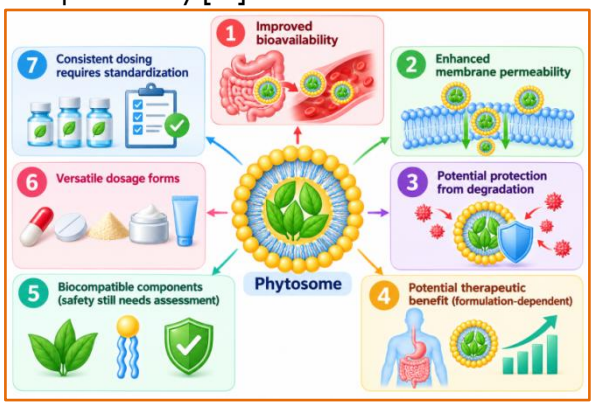


Figure 03: Advantages of phytosomes

Potential Protection against Degradation: Complex formation may help protect susceptible compounds from oxidation, hydrolysis, or other degradation processes. The extent of protection depends on the active constituent and storage conditions [34].

Improved Therapeutic Performance: Increased exposure to an active compound may improve its pharmacological effects in certain settings. A reduction in required dose or improvement in clinical outcomes must be established for each formulation rather than assumed [35].

Biocompatible Components: Phospholipids such as phosphatidylcholine are commonly used and supports biocompatibility, although the complete formulation still requires safety assessment [7].

Versatility in Dosage Forms: Phytosome-based ingredients may be incorporated into capsules, tablets, powders, topical creams, gels, and other suitable formulations, depending on their physical and chemical properties [20].

Potential Reduction in Dose Variability: A standardized phytosome formulation may provide more consistent delivery than a poorly standardized herbal extract. Batch-to-batch consistency must be demonstrated through appropriate quality-control procedures [7].

Disadvantages

Higher formulation costs: Phospholipid selection, solvent processing, specialized equipment, and quality testing may increase production costs [36].

Formulation complexity: The active compound, phospholipid type, molar ratio, temperature, and processing conditions require optimization [20].

Potential lipid oxidation: Unsaturated phospholipids may undergo oxidation, affecting formulation quality and shelf life [37].

Variable performance: They can respond differently to complexation, making a single formulation strategy unsuitable for all plant extracts [20].

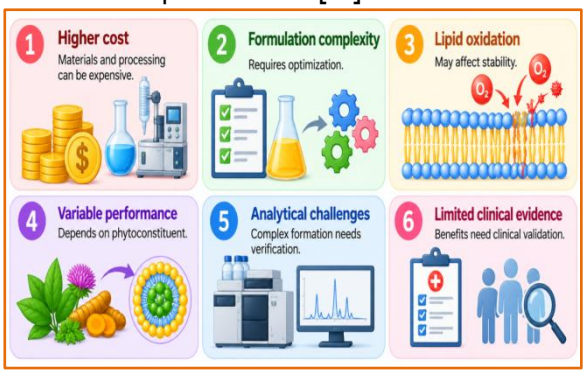


Figure 03: Disadvantages of phytosomes

Analytical difficulties: distinguishing a genuine molecular complex from a physical mixture requires appropriate analytical techniques [19].

Possible gastrointestinal variability: Food intake, digestive conditions, and individual physiological differences can influence absorption of orally administered formulations.Limited clinical evidence for some products: promising preclinical findings do not necessarily translate into clinically meaningful benefits [22].

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Limitations and challenges

Selection and Standardization of Phytoconstituents: Plant extracts may contain numerous compounds with different molecular weights, polarities, and functional groups. Only suitable constituents may form effective complexes with phospholipids. Variations in plant species, cultivation,

harvesting, extraction, and storage can also affect the chemical composition of herbal ingredients [25].

Stability and Shelf Life: Phospholipids and plant-derived compounds may be sensitive to oxygen, moisture, light, and temperature. Researchers must establish appropriate storage conditions and evaluate the stability of the active ingredient and complex throughout the intended shelf life [21].

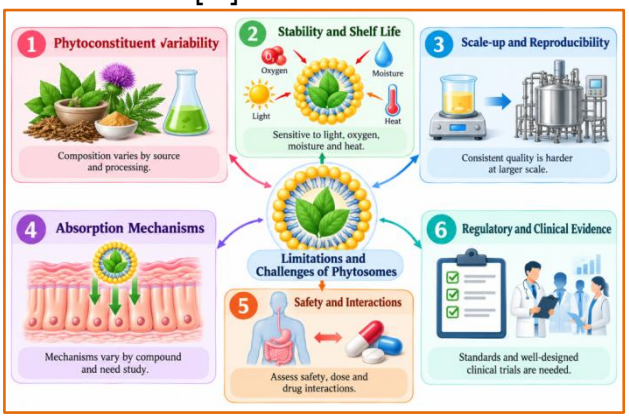


Figure 04: Limitations and challenges of phytosomes

Scale-up and Manufacturing Reproducibility: Laboratory-scale preparation may not translate directly to industrial production. Maintaining consistent particle characteristics, complexation, residual-solvent levels, and active-compound content at larger scales can be difficult [27].

Incomplete Understanding of Absorption Mechanisms: Although phospholipid complexation can enhance delivery, the precise mechanism varies between compounds. Improved performance may arise from changes in solubility, membrane partitioning, protection from degradation, or other factors. These mechanisms require compound-specific investigation [20, 27].

Safety and Drug Interactions: Improved absorption may increase systemic exposure and potentially alter adverse-effect profiles or interactions with concomitant medicines. Safety evaluation should include the active phytoconstituent, phospholipid, excipients, and any impurities or degradation products [28].

Regulatory and Clinical Challenges: Regulatory requirements differ according to whether a product is developed as a medicine, botanical drug, dietary supplement, or cosmetic. Evidence requirements, quality standards, and permitted health claims may therefore differ. Well-designed clinical trials are needed to establish efficacy, safety, appropriate dosage, and long-term outcomes [15, 28].

Applications

Liver Protection/Hepatoprotective Applications: Silymarin and silybin are studied for improving absorption and supporting liver-protective effects. Further clinical studies are needed to confirm their benefits [17, 22, 37].

Reducing Inflammation and Oxidative Stress: Curcumin and other polyphenol may improve the delivery of compounds with antioxidant and anti-inflammatory properties, potentially helping manage inflammation and oxidative stress [7, 17, 28].

Heart and Metabolic Health: Flavonoids and polyphenols are investigated for their possible effects on cholesterol levels, blood glucose regulation, and cardiovascular health [17, 18, 28].

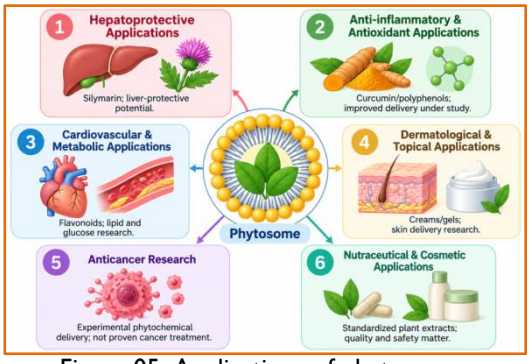


Figure 05: Applications of phytosomes

Nutritional Supplements and Cosmetics: To improve the delivery of selected plant-derived ingredients. Their safety, quality, and claimed benefits require proper evaluation [38, 39].

Cancer Research: Improve the delivery and availability of phytochemicals such as curcumin. However, experimental findings do not prove that these formulations can prevent or treat cancer in humans [7, 40].

Skin Care and Topical Delivery: Incorporated into creams and gels to improve the delivery of plant-based compounds into the skin, supporting research into skin protection and local treatment [41, 42].

Safety and Need for Clinical Studies: Requires testing for safety, stability, and quality. Well-designed clinical studies are essential to establish its effectiveness and identify possible adverse effects [7, 20, 43].

Preparation Methods

In the solvent evaporation method, the phytoconstituent and phospholipid are dissolved, mixed to promote complex formation, and the solvent is removed [7, 13]. The antisolvent precipitation method involves adding an antisolvent to the dissolved mixture, followed by collection and drying of the precipitated complex [44, 45]. Thin-film hydration involves forming a lipid film and hydrating it to produce dispersed lipid structures; genuine phytosome formation must be confirmed analytically [27, 46]. Mechanical and advanced techniques, including high-shear mixing, homogenization, and sonication, improve dispersion and help control particle size according to formulation requirements [25, 38, 47, 48].

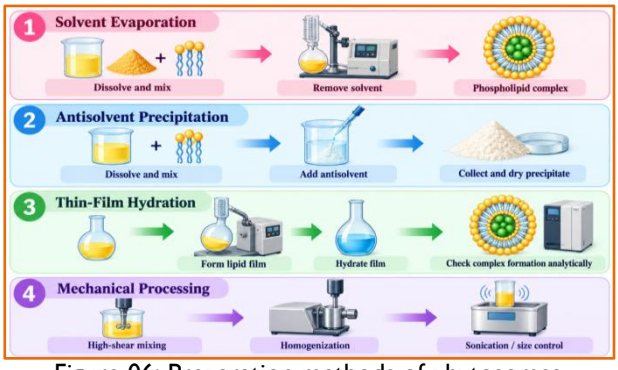


Figure 06: Preparation methods of phytosomes

Characterization

Proper characterization is essential to establish the quality, reproducibility, and performance of a phytosome formulation. No single analytical technique is sufficient to prove complex formation [25, 27, 59-61].

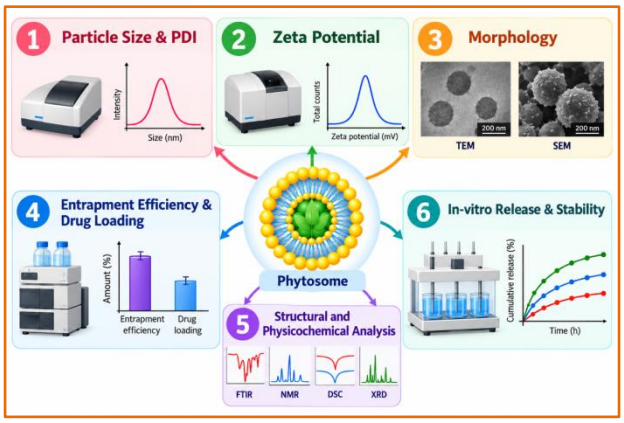


Figure 07: Characterization methods of phytosomes

Complementary methods should be selected according to the formulation, and comparisons should include the un-complexed phytoconstituent and a physical mixture where appropriate [7].

Table 01: Characterization methods and evaluation parameters

S. No.	Parameter	Method / instrument	Purpose
1	Particle size and size distribution	Dynamic light scattering (DLS)	Determines average particle size and size distribution of the formulation [49].
2	Polydispersity index (PDI)	DLS	Evaluates the uniformity of particle size distribution [50].
3	Zeta potential (ZP)	Electrophoretic light scattering	Measures surface charge and help assess colloidal stability [51].
4	Morphology and surface characteristics	Transmission electron microscopy (TEM), scanning electron microscopy (SEM), or atomic force microscopy (AFM)	Examines particle shape, surface appearance, and structural features[52].
5	Phytoconstituent–phospholipid interaction (Compatibility studies)	Fourier-transform infrared spectroscopy (FTIR) and nuclear magnetic resonance (NMR)	Investigates functional-group changes and molecular interactions associated with complex formation[53]
6	Thermal properties	Differential scanning calorimetry (DSC)	Evaluates thermal behaviour of the phytoconstituent and phospholipid complex [54].
7	Crystallinity	X-ray diffraction (XRD)	Assesses changes in crystalline or amorphous characteristics after complex formation [55].
8	Phytoconstituent content	High-performance liquid chromatography (HPLC) or UV–visible spectrophotometry	Quantifies the active constituent in the formulation using a suitable validated method[56].
9	Complexation or entrapment efficiency	Separation of free constituent followed by HPLC or spectrophotometric analysis	Estimates the proportion of the phytoconstituent associated with the formulation [57].
10	Drug loading	Quantitative assay and formulation mass measurement	Determines the amount of phytoconstituent present relative to the total formulation or carrier mass [58].
11	In-vitro release	Dialysis, dissolution, or another validated release method	Evaluates the release profile of the under specified experimental conditions [59-63].
12	Stability and shelf life	Periodic measurement of particle size, PDI, zeta potential, active content, and physical appearance	Identifies changes during storage and helps establish formulation stability [63].
13	Formulation optimization	Design of experiments (DoE) and quality-by-design (QbD) approaches	Study the effects of formulation and process variables on critical quality attributes [49-52].

FUTURE PERSPECTIVES

Advanced Formulation Development: The use of optimized phospholipids, improved processing methods, and rational formulation design may enhance product quality and reproducibility. Researchers should establish clear relationships between composition, manufacturing conditions, and performance [21].

Quality-by-Design Approaches: Quality-by-design principles and systematic experimental designs can help identify critical material attributes and manufacturing parameters. Such approaches may improve scale-up, reduce batch variability, and support consistent product quality [23, 25].

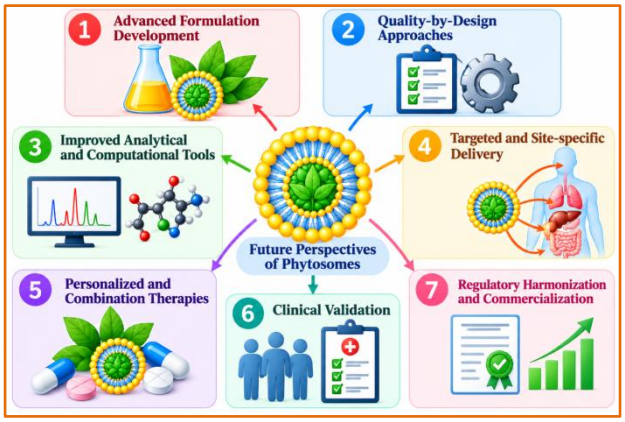


Figure 08: Future perspectives of phytosomes

Improved Analytical and Computational Tools: Advanced spectroscopic techniques, molecular modeling, and computational methods may help explain phytoconstituent–phospholipid interactions and guide the selection of suitable ingredients [23-27].

Targeted and Site-specific Delivery: Combining phytosome technology with appropriate surface modifications or other delivery strategies may support site-specific delivery. Targeted delivery must be demonstrated experimentally rather than inferred from particle size or composition alone [28].

Personalized and Combination Therapies: Future investigations may explore phytosomes containing standardized combinations of phytochemicals or their use alongside established therapies. Such approaches require rigorous evaluation of compatibility, pharmacokinetics, interactions, and clinical outcomes [15].

Clinical Validation: Well-designed randomized controlled trials should compare phytosome formulations with suitable reference products, assess clinically relevant endpoints, and monitor adverse effects. Long-term safety, dose selection, and the relationship between increased bioavailability and therapeutic benefit also require investigation [15].

Regulatory Harmonization and Commercialization: Clear specifications for phytochemical content, phospholipid composition, complex formation, impurities, stability, and batch consistency will be important for wider commercialization. Standardized testing and transparent reporting can strengthen confidence in phytosome-based products [64-67].

CONCLUSION

Phytosomes represent a promising approach for bridging traditional herbal medicine and modern drug delivery technology. By forming complexes between selected phytoconstituents and phospholipids, this technology may improve the absorption, bioavailability, stability, and delivery performance of plant-derived compounds. Research involving silymarin, curcumin, flavonoids, and other phytochemicals have demonstrated potential across pharmaceutical, nutraceutical, and cosmetic applications.Nevertheless, phytosomes are not universally effective, and their performance depends on the chemical properties of the active compound, formulation composition, preparation method, and route of administration. Manufacturing reproducibility, lipid oxidation, regulatory requirements, safety, and insufficient clinical evidence for some indications remain important challenges. Future progress will depend on rigorous characterization, standardized manufacturing, formulation-specific pharmacokinetic studies, and well-designed clinical trials. With continued scientific development, phytosome technology may contribute to more reliable and effective delivery of selected herbal bioactives.

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The authors have no acknowledgements to declare.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

INFORMED CONSENT

Informed consent was obtained from all authors, as applicable.

ETHICAL STATEMENT

Not applicable.

AUTHOR CONTRIBUTIONS

Not Declared.

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